REMARKS

Claims 20-24 and 26-43 are pending in the application. Claims 39 and 40 are allowed. Claim 26 is withdrawn from consideration by the Examiner. Claims 20, 28-35, 37, 38, 41 and 42 stand rejected. Claims 21-24, 26, 27, and 43 are objected to. The action is made final.

Reconsideration of the withdrawal of claim 26 is respectfully requested.

Claims 20, 28, and 29 are amended herein.

Item 4a. Applicants respectfully thank the Examiner for withdrawal of the nonstatutory obviousness-type double patenting rejections of claims 20-35, 37, and 41-43.

Item 4b. Applicants respectfully acknowledge withdrawal of rejections of claims 27 and 39-40 under 35 U.S.C. § 112 (1). The Examiner states that, with regard to claim 27, "the recitation of 95% identify with functional language is within the scope of the enabled embodiments."

Item 4c. Applicants thank the Examiner for withdrawal of rejection of claims 20 and 26 under 35 U.S.C. § 112(2).

Rejections under 35 U.S.C. § 112 (1) – Enablement

Item 5a. Claims 20, 28-35, 37-38 and 41-43 stand rejected under 35 U.S.C. § 112(1) because, the Examiner asserts: "the specification, while being enabled for an isolated polynucleotide comprising a sequence set forth in SEQ ID NO: 11 encoding the protein comprising the amino acid sequence set forth in SEQ ID NO: 2 [sic, 12] a host cell that has been genetically engineered by the incorporation expressibly therein of said polynucleotide, and a method of identifying ligands for GLP-2 by using said cell, does not reasonably provide enablement for a mammalian homolog or variant of the polynucleotide of SEQ ID NO: 12, or a polynucleotide which is at least 80%, 90% or 95% sequence identity which selectively binds to GLP-2."

Applicant respectfully traverses the rejection for reasons of record. Never-the-less, to speed prosecution, claim 20 has been amended to incorporation the elements of claim 27 in accordance with Examiner's comment that claim 27 is enabled. See item 4b. Thus, one element of claim 20 as amended is limited to a GLP-2 receptor which is at least 95% identical to amino acids 26-553 of SEQ ID NO:12. Moreover, element (c), directed to a variant GLP-2, has been deleted.

All amendments are made without prejudice or disclaimer. Applicant reserves the right to seek broader claims in a separate application.

Accordingly, claim 20, as amended, is fully enabled by the specification and allowable.

With regard to claims 28-31, the Examiner rejects the claims for lack of enablement, asserting that the conditions disclosed on pages 22 and 27 of the specification are not high stringency conditions.

Claims 28 and 29 have been amended to recite that the polynucleotides are 90% identical or more. Support for this definition of high stringency is found on page 7, lines 4-6 of the specification. One of ordinary skill in the art could readily choose experimental conditions that accord with this limitation. It is believed that these amendments obviate the rejections.

Rejections under 35 U.S.C. § 112(1) – Written Description

Item 5b. Claims 20, 28-35, 37-38 and 41-42 are now rejected for lack of written description. The Office Action asserts in the referenced Office Action of August 23, 2006, that "the claims are drawn to a genus of polynucleotides that is defined only by sequence identity. *At* 10. The Office Action further states:

> To provide evidence of possession of a claimed genus, the *specification* must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties,

> functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case the only factor present *in the claim* is a partial structure …

Id. (Emphasis added.)

The highlighted text above identified that the written description requirement is directed to the specification, not the claims.

Applicants respectfully assert that the claims as amended have very substantial written description in the specification, as described in detail below.

With regard to disclosure of *complete or partial structure*, the specification discloses that a "cDNA of human origin, SEQ ID NO:11, encodes the full length human GLP-2 receptor having residues 67-533 of SEQ ID NO: 12." *At* 6. Thus the complete and unambiguous chemical formula is provided for a first claimed embodiment of the invention.

The specification reports a second complete chemical structure according to claim 20, as amended, at page 6, lines 21-23.

A third complete GLP-2 receptor chemical structure is reported as the point mutation corresponding to human [Glu ^{85}]-GLP-2 receptor. *At* 10, ll. 8-14.

Further with regard to disclosure of *chemical structure*, the specification teaches that human GLP-2 receptor precursor is a single polynucleotide chain of 553 amino acids having a total molecular weight of 72 kDa. *At* 6, ll. 4-6. The specification discusses GLP-2 receptor signal sequences. *At*, ll. 6-9. Moreover, the specification teaches cleavage of the precursor to form a mature functional receptor. *At* 6, ll. 9-11. The GLP-2 receptor according to claim 20, as amended, likely has a first transmembrane region (TM I: residues 181-203), a second transmembrane region (TM II: residues 211-230), a third transmembrane region (TM III: residues 262-285), a fourth transmembrane region (TM IV: residues 300-321), a fifth transmembrane region (TM V: residues 339-362), a sixth transmembrane region (TM VI:

residues 386-405), and a seventh transmembrane region (TM VII: residues 422-441). *At* 6, ll. 9-17. One of ordinary skill in the art would recognize how these structural features limit possible amino acid substitutions.

The specification provides yet further written description of claim 20, as amended, in that the region of the N-terminal extracellular domain is suggested to comprise about residues 67 to 181. *At* 6, ll. 17-21 and 11-17.

Moreover, the structure of the receptor of claim 20, as amended, is also disclosed to have an intracellular C-terminal portion likely corresponding to residues 442-553. *At* 6, ll. 17-21.

The specification also notes that the seven transmembrane regions are hydrophobic and interspersed with six short hydrophilic domains. *At* 6, ll. 17-21. Thus, the inventors were cognizant of a series of complex structures with identifiable domains each of which had functional features such as hydrophobicity and structural features such as exemplary amino acid sequence.

With regard to written description of *physical and/or chemical properties*, it was noted above that some domains in the sequence claimed in claim 20, as amended, are hydrophobic and some are hydrophilic. Based on common knowledge, and the detailed disclosure in the specification, one of skill in the art would recognize that the inventors have identified useful properties that characterize the claimed receptors and the polynucleotides which encode them.

Further with regard to written description of *physical and/or chemical properties*, the specification discloses that the receptor encoded by the polynucleotide of claim 20, as amended, should have a molecular weight of about 72kDa. *At* 6, ll. 4-6.

With regard to written description of *functional characteristics* the specification teaches that the receptor of claim 20, as amended, is capable of selectively binding GLP-2. *At* 4, ll. 1-3.

Furthermore, the claimed receptor, when appropriately expressed in a cell or a cell membrane, has the functional property of responding to GLP-2. *At* 4, ll. 3-5.

The specification further teaches that GLP-2 receptor-mediated *functional* responses to GLP-2 can include D-glucose transport (p. 1, ll. 14-16), proliferation of the epithelium of the small intestine (p. 1, ll. 11-13), modulation of cyclic AMP levels (p. 4, ll. 5-10), mobilization of calcium (p.4, ll. 5-10), change in inositol phospholipid hydrolysis (p. 4, ll. 5-10), and modulation of guanylyl cyclase activity (p. 4, ll. 5-10).

With regard to written description of *structure/function correlations*, the specification teaches that the form of receptor claimed in claim 20, amended, can have a substitution of glutamate for the arginine at position 85 without destroying receptor function. *At* 10, ll. 8-13.

Many more *structure/function* correlations would be evident to one skilled in the art upon reading the specification and comparing details of the structures of the several functional receptors provided, including rat GLP-2 receptor, rat GLP-2 receptor precursor, and human GLP-2 receptor precursor.

With regard to written description of *methods of making the claimed product*, isolation and screening of natural receptors is disclosed on page 8 and following. Synthetic variants are also disclosed along with a method of making them are disclosed on page 9 and following. Preferred sites for substitution of amino acids are also disclosed. *At* 10, ll. 3-4.

Thus, the specification provides extensive disclosure directed at every one of the factors identified by the Examiner: *complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlations, methods of making the claimed product*, and by inference, *combinations* of these factors.

Thus, unlike *Fiddes*, in which a single sequence was shown, the instant specification shows three complete sequences that are within the scope of claim 20 as amended. *Fiddes v. Baird,* 30 USPQ2d 1481 (Board Pat. App. Int. 1994). From the detailed disclosure, one of skill in the art can readily determine that some domains are functionally inactive. Moreover, comparison of the rat and human sequence shows conserved regions and residues and variable

regions. Furthermore, some specific amino acids can be substituted without degrading the receptor activity.

It is unnecessary and not even desirable to recite every species within the genus because one of skill in the art would recognize from the disclosure of the three species mentioned above that the inventors had possession of the invention as claimed in claim 20, amended.

Applicants respectfully suggest that there is overwhelming evidence recited above that the inventors possessed the full scope of claim 20, as amended, and of claims 28-35, 37-38, and 41-42, which depend from claim 20.

With regard to claim 29, the Examiner states that an oligonucleotide that comprises at least 15 nucleotides and also hybridizes to the polynucleotide recited in claim 20, would not be expected to encode the proteins recited in claim 20. Office Action *at* 8.

The Examiner is quite correct: The claim is drawn to screening probes, not coding sequences. Applicant respectfully directs Examiner's attention to the specification which discloses that oligonucleotides of at least 15 nucleotides are useful for screening cDNA libraries. Specification *at* 8.

Rejections under 35 U.S.C. § 112(2)

Item 6. Claims 28-31 stand rejected as indefinite in the recitation of "hybridizes under conditions of high stringency." The claims have been amended to recite that the polynucleotides are 90% identical or more. This structural limitation constrains the conditions used for high stringency hybridization and clearly indicates to one of ordinary skill in the art the kinds of hybridization conditions that are suitable. Thus, it is believed, the claims are allowable.

Claim Objections

Claims 21-24, 26, 27, and 43 stand objected to as dependent upon a rejected claim, but allowable if rewritten in independent form.

Claim 20 has been amended to incorporate the limitations of claim 27. Claims 21-24, 26, and 43 depend directly or indirectly from claim 20. Consequently claims 21-24, 26, 27 and 43 should be allowable on these grounds.

Other Issues

Reconsideration of the withdrawal of claim 26 is respectfully requested. The claim appears to have been withdrawn in error in the Office Action.

Applicants acknowledge and thank the Examiner for allowance of claims 39 and 40.

Conclusion

For at least the reasons provided above, all pending claims, as amended, should be allowable.

No fee is due with this timely filing. If a fee is due, please charge our Deposit Account No. 22-0185, under Order No. 22316-00029-US2 from which the undersigned is authorized to draw. If direct communication with the undersigned would facilitate prosecution, please telephone at 202-331-7111.

Dated: May 18, 2007

Respectfully submitted,

Electronic signature: /Thor B. Nielsen/
Thor B. Nielsen
Registration No.: 45,528
Mark J. Pino
Registration No.: 43,858
CONNOLLY BOVE LODGE & HUTZ LLP
1990 M Street, N.W., Suite 800
Washington, DC 20036
(202) 331-7111 (Tel)
(202) 293-6229 (Fax)
Attorneys for Applicant